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- b) an angling mechanism that sets the angle of the flat membranes at a respective non-zero angle relative to the plane of the plate, the respective angles decreasing as the position of the respective wells increases relative to a line perpendicular to an axis of rotation about which the plate rotates, the line passing through the center of a plane of the plate.

Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i-iii).

Please add new Claims 80-82, as follows:

80. (New) The device of Claim 78 wherein the angling mechanism includes a support device which can hold the flat membrane for filtering a fluid at a non 90° angle relative to the line.
81. (New) The device of Claim 80 wherein the angling mechanism includes a wedge.
82. (New) The device of Claim 78 wherein the angling mechanism is located outside of the plate.

#### REMARKS

Claims 42, 62, and 71 have been canceled.

Claims 38, 39, 41, 43, 45, 50, 55-57, 59, 64-66, 68, and 79 have been amended to recite that the membrane is "flat." Support for these amendments can be found throughout the specification, the figures, and originally filed claims, for example, at page 7, lines 8-11; at page 7, lines 24-26; at page 8, lines 8-11; at page 11, lines 23-29; and in Figures 4-6 and 11.

Claims 38, 41, and 79 have been amended to recite that the membrane is "at the bottom of a storage chamber." Support for these amendments can be found throughout the specification, the figures, and originally filed claims, for example, page 7, lines 5-20; page 11, line 20 to page 12, line 5; and Figures 4 and 11.

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Claim 15 has been amended to including the word "the" before the word "plate." This corrects an inadvertent typographical error.

New Claim 80 includes the elements of Claims 39 and is directed to a support device which can hold the flat membrane for filtering a fluid at a non 90° angle relative to the line. Support for new Claim 80 can be found throughout the specification, the figures, and the originally filed claims, for example, at page 8, lines 7-12; page 11, lines 23-27; page 13, lines 10-11, and Figures 6 and 11.

New Claim 81 includes the elements of Claims 40 and is directed to a wedge. Support for new Claim 81 can be found throughout the specification, the figures, and the originally filed claims, for example, at page 2, line 28; page 3, lines 22-23; page 4, lines 27-28; page 8, lines 9-10; and Figure 6.

New Claim 82 is directed to an angling mechanism located outside of the plate. Support for new Claim 82 can be found throughout the specification, the figures, and the originally filed claims, for example, at page 2, line 28; page 3, lines 22-23; page 4, lines 27-28; page 8, lines 9-10; and Figure 6.

No new matter has been added.

Claims 38-41, 43-45, 50-62, 63-70, 72, and 74-82 are currently pending. A corresponding number of claims have been cancelled for the number of claims added.

#### Applicants' Invention

In order to address the novelty and obviousness rejections set forth in the Office Action, Applicants believe it would be helpful to reiterate the claimed invention.

Multi-well filtration plates are commonly used to filter fluids. If the fluid is sufficiently viscous, the plates are often placed in a centrifuge in order to force the fluid through the filter material. However, the amount of fluid actually filtered in each of the wells is not always equal. Generally, the outer wells of the plate have more filtrate volume and the inner rows of the plate have the least amount of filtrate, thereby causing an uneven filtrate distribution or "smile effect," as shown in Figure 1 of the Application.

Applicants have made the surprising and non-obvious discovery that different forces affect the wells of a multi-well filtration plate when it is centrifuged in a swinging bucket rotor, and these forces give rise to the "smile effect." Applicants' invention identifies, characterizes, and offers multiple solutions to this problem to achieve uniform filtrate volumes in all wells.

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Applicants' invention relates to methods, systems, and devices for reducing the "smile effect" to provide an even distribution of filtrate in each well across the plate. In some embodiments, Applicants' invention provides an angling mechanism that can adjust the angle of the plate to a non 90° angle relative to a line wherein the line is perpendicular to the axis of rotation of the centrifuge and passes through the center of a major plane of the plate. The angle controls the force vector tangential to the membrane.

Applicants' invention provides the advantage that it can increase average volume filtered during centrifugation. The filtrate volume is substantially uniform with little well-to-well filtrate volume variability, thereby minimizing the "smile effect." The angling mechanism can increase the average filtrate flow rate among a plurality of wells in a filtration well plate.

Rejection of Claims 38-45, 50, 51, 53-59, 61, 63-68, 70, 73, 74, and 76-78 under 35 U.S.C. § 102(a) in View of WO 00/35565

Claims 38-45, 50, 51, 53-59, 61, 63-68, 70, 73, 74, and 76-78 are rejected under 35 U.S.C. § 102(a) as being anticipated by WO 00/35565.

WO 00/35565 disclose an ultrafiltration device that has a filter membrane sealed inside a tubular reservoir body. The membrane is sealed to the tubular body along a closed contour in such a manner that the filter forms a conical shape. In other words, the membrane taught in WO 00/35565 is curved.

Without agreeing with the Examiner that WO 00/35565 anticipates Applicants' claimed invention, Applicants have amended Claims 38, 39, 41, 43, 45, 50, 55-57, 59, 64-67, 68, and 79 to recite a flat membrane. WO 00/35565 does not teach a flat membrane nor an angling mechanism as claimed by Applicants.

In addition, Claim 78 recites a "membrane being coplanar with the plate." WO 00/35565 does not disclose membranes that are coplanar with a plate.

In light of these arguments as well as the amendments to the independent claims, and hence all the dependent claims, Applicants' claimed invention is not anticipated by WO 00/35565.

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Rejection of Claims 38-45, 50, 51, 53-57, 63-66, 73, 76, and 78 under 35 U.S.C. § 102(b) in View of Stankowski, et al.

Claims 38-45, 50, 51, 53-57, 63-66, 73, 76, and 78 are rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Patent No. 5,674,395, issued to Stankowski, et al.

Stankowski, et al. disclose a multi-well filtration device in which at least one side wall includes one or more filtration membranes.

Without agreeing with the Examiner that Stankowski, et al. anticipate Applicants' claimed invention, Applicants have amended Claims 38, 41, and 79 to recite a flat membrane at the bottom of a storage chamber. Stankowski, et al. do not teach a flat membrane at the bottom of a storage chamber nor an angling mechanism as claimed by Applicants. Further, the flat membrane at the bottom of the storage chamber can allow the chamber to filter to dryness. The device in Stankowski, et al. has a dead stop region in which a portion of the fluid does not flow from the chamber.

In addition, Claim 78 recites a "membrane being coplanar with the plate." Stankowski, et al. do not disclose coplanar membranes.

In light of these points as well as the amendments to the independent claims, and hence all the dependent claims, Applicants' claimed invention is not anticipated by Stankowski, et al.

Rejection of Claims 60, 62, 69, 71, 72, 75, and 79 under 35 U.S.C. § 103(a) in View of WO 00/35565

Claims 60, 62, 69, 71, 72, 75, and 79 are rejected under 35 U.S.C. § 103(a) as being obvious in light of WO 00/35565.

Examiner states that WO 00/35565 discloses the claimed invention with the exception of the exact angle of the membranes (Claims 60, 69, 72, 75, and 79) and the exact number of wells (Claims 62 and 71). Examiner believes it would have been obvious to one of ordinary skill in the art at the time the invention was made to angle the membranes as taught in WO 00/35565 in the manner recited in Claims 60, 69, 72, 75, and 79 because Examiner believes WO 00/35565 discloses a range which overlaps these values (WO 00/35565, pg. 12, lines 8-11). Examiner also believes the exact number of wells employed in the system taught in WO 00/35565 (pg. 12, lines 17-18) will not materially affect the overall operation of the referenced device or to produce any new and unexpected result. Therefore, Examiner deemed the number of wells employed to be an obvious matter of choice in design, insufficient to patentably distinguish claims 62 and 71.

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WO 00/35565 does not teach or suggest a plurality of wells within a plate wherein each well includes a flat membrane at the bottom of a storage chamber. Further, WO 00/35565 does not teach or suggest that the centrifugation of a plate with a series of wells can result in disparate filtration rates in the individual wells.

Applicants have made the surprising discovery that different forces affect the wells of a multi-well filtration plate when it is centrifuged in a swinging bucket rotor. It is not obvious that these forces give rise to the "smile effect." Since WO 00/35565 does not even mention an uneven distribution and the resulting "smile effect," one skilled in the art would not have been motivated by its teachings to address its disadvantages. Even if WO 00/35565 had alluded to the "smile effect," there is no teaching or suggestion that an angling mechanism would alleviate it.

Because WO 00/35565 does not teach or suggest a plurality of wells within a plate wherein each well includes a flat membrane at the bottom of a storage chamber and does not teach or suggest the "smile effect," Applicants' claimed invention is not obvious in view of WO 00/35565.

Rejection of Claims 60, 69, 72, 75, and 79 under 35 U.S.C. § 103(a) in View of Stankowski, et al.

Claims 60, 69, 72, 75, and 79 are rejected under 35 U.S.C. § 103(a) as being obvious in light of Stankowski, et al.

Examiner stated that Stankowski, et al. discloses the claimed invention with the exception of the exact angle of the membrane. Examiner concluded that it would have been obvious to one of ordinary skill in the art at the time the invention was made to angle the membranes of the system taught in Stankowski, et al. in the manner recited in Claims 60, 69, 72, 75, and 79, since Examiner believes that Stankowski, et al. discloses a range which overlaps the claimed values.

As with WO 00/35565, Stankowski, et al. does not teach or suggest a plurality of wells within a plate wherein each well includes a flat membrane at the bottom of a storage chamber. Stankowski, et al. does not teach or suggest that the centrifugation of a plate with a series of wells can result in disparate filtration rates in the individual wells.

Applicants have made the surprising discovery that different forces affect the wells of a multi-well filtration plate when it is centrifuged in a swinging bucket rotor. It is not obvious that these forces give rise to the "smile effect." Since Stankowski, et al. does not even mention the

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"smile effect," one skilled in the art would not have been motivated by its teachings to address the disadvantages produced by the "smile effect." Even if Stankowski, *et al.* had alluded to the "smile effect," there is no teaching or suggestion that an angling mechanism would alleviate it.

Therefore, Applicants' claimed invention is not obvious in view of Stankowski, *et al.*

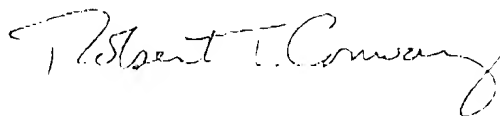
#### CONCLUSION

Applicants' claimed invention is not anticipated or made obvious by the teachings of either WO 00/35565 or Stankowski, *et al.* individually or in combination. Reconsideration and withdrawal of the rejections is requested.

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner believes that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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MARKED UP VERSION OF AMENDMENTSClaim Amendments under 37 C.F.R. § 1.121(c)(1)(ii)

38. (Twice Amended) A fluid filtering device comprising:
- a) a plurality of filtering wells within a plate wherein each filtering well includes a flat membrane at the bottom of a storage chamber for processing a fluid; and
  - b) an angling mechanism, wherein the angling mechanism sets the angle of the flat membranes within the plurality of filtering wells at a non 90° angle relative to a line perpendicular to an axis of rotation about which the plate rotates, the line passing through the center of a plane of the plate.
39. (Amended) The device of Claim 38 wherein the angling mechanism includes a support device which can hold the flat membrane for filtering a fluid at a non 90° angle relative to the line.
41. (Amended) A fluid filtering device comprising:
- a) a plurality of wells within a plate wherein each well includes a flat membrane at the bottom of a storage chamber for filtering a fluid; and
  - b) an angling mechanism wherein the angling mechanism sets the angle of one or more of the flat membranes at a non-zero angle relative to the plane of the plate.
43. (Amended) The device of Claim 41 wherein the angle relative to the plane of the plate includes a side-to-side orientation of the flat membrane.
45. (Amended) The device of Claim 41 wherein each flat membrane in each well includes an individually specified angle relative to the plane of the plate.
50. (Amended) The device of Claim 41 wherein the angling mechanism includes a support device which can hold the flat membrane for filtering a fluid at a non zero-angle relative to the plane of the plate.

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55. (Amended) The device of Claim 41 wherein the plane of the flat membranes are at a non-zero angle relative to the plane of the plate.
56. (Amended) The device of Claim 41 wherein the flat membrane includes a microfiltration membrane.
57. (Amended) The device of Claim 41 wherein the flat membrane includes an ultrafiltration membrane.
59. (Amended) The device of Claim 58 wherein the angles of the flat membranes within a row are substantially the same.
64. (Amended) The device of Claim 38 wherein the planes of the flat membranes are at a non 90° angle relative to the line.
65. (Amended) The device of Claim 38 wherein the flat membrane includes a microfiltration membrane.
66. (Amended) The device of Claim 38 wherein the flat membrane includes an ultrafiltration membrane.
68. (Amended) The device of Claim 67 wherein the angles of the flat membranes within a row are substantially the same.
72. (Amended) A fluid filtering device comprising:
- a) a plurality of filtering wells within a plate, each well including a flat membrane at the bottom of a storage chamber for processing a fluid; and
  - b) an angling mechanism that sets the angle of the flat membranes at a respective non-zero angle relative to the plane of the plate, the respective angles decreasing as the position of the respective wells increases relative to a line perpendicular to an axis of rotation about which the plate rotates, the line passing through the center of a plane of the plate.